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10/510,596	08/17/2005	Masayuki Ii	084437-0184	1802

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EXAMINER	
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1617	

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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/510,596	II ET AL.	
	Examiner	Art Unit	
	Shobha Kantamneni	1617	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *16 June 2009*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-20* is/are pending in the application.

4a) Of the above claim(s) *7-20* is/are withdrawn from consideration.

5)☒ Claim(s) *NONE* is/are allowed.

6)☒ Claim(s) *1-6* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *10/07/2004*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Claims 1-20 are pending.

Election/Restrictions

Claims 7-20 are withdrawn from consideration pursuant to 37 CFR 1.142(b), as being drawn to nonelected inventions.

Applicant's election of invention Group I, claims 1-6, in the reply filed on 06/16/2009 is herein acknowledged. Applicants elect the species of compound 72 as a non-peptide compound of formula I or II, and an antibacterial agent as a drug in claim 4. Because applicant did not distinctly and specifically point out the supposed errors in the restriction requirement, the election has been treated as an election without traverse (MPEP § 818.03(a)). The requirement is made FINAL.

Claims 1-6 read on the elected Group and species. Claims 1-6 are examined herein so far as they read on the elected species.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 1-6 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for a method of treatment of severe sepsis comprising administering an effective amount of a particular compound of formula (I) or

formula (II), does not reasonably provide enablement for a method for **prophylaxis of severe sepsis**. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to practice the invention **commensurate in scope** with these claims.

The instant specification fails to provide information that would allow the skilled artisan to practice the instant invention without undue experimentation. Attention is directed to *In re Wands*, 8 USPQ2d 1400 (CAFC 1988) at 1404 where the court set forth the eight factors to consider when assessing if a disclosure would have required undue experimentation. Citing *Ex parte Forman*, 230 USPQ 546 (BdApls 1986) at 547 the court recited eight factors:

> (1) the nature of the invention; (2) the state of the prior art; (3) the relative skill of those in the art; (4) the predictability or unpredictability of the art; (5) the breadth of the claims; (6) the amount of direction or guidance presented; (7) the presence or absence of working examples; and (8) the quantity of experimentation necessary.

(1) The Nature of the Invention:

The rejected claims are drawn to an invention which pertains to a method of treating or preventing sepsis.

(2) State of the Prior Art:

The state of the art regarding treating sepsis is relatively high, however the state of the art for the prevention of sepsis is non-existent.

(3) Breadth of Claims:

The complex nature of the subject matter of this invention is greatly exacerbated by the breadth of the claims. The claims encompass the prevention or treatment of severe sepsis .

(4) Guidance of the Specification:/ (5) Working Examples:

The guidance of the specification as to the prevention of sepsis is completely lacking. The specification discloses preventing the onset of sepsis. However, the specification fails to mention how one is able to determine whether the onset of sepsis in a subject would have occurred in the absence of treatment, thus being unable to confirm that prevention has indeed taken place. Moreover, the specification fails to mention the complete prevention or cessation of sepsis once the onset of preclinically evident stage is determined.

(6) The Relative Skill of those in the Art:

One of ordinary skill in the art does not know how to prevent sepsis. Moreover, one is unable to determine whether a subject will ever develop sepsis should this subject be administered the anti-sepsis drug.

(7) The Predictability or Unpredictability of the Art:

The invention is directed to a method of treating or preventing sepsis. The specification does not disclose how one of ordinary skill in the art at the time of the invention would be able to prevent sepsis, nor does the prior art reveal any type of prevention associated with sepsis.

The relative skill in the art and predictability is low with respect to prophylaxis of severe sepsis, “prophylaxis” actually means “To prevent”, which actually means to

anticipate or counter in advance, to keep from happening etc. (as per Webster's II Dictionary). Pharmacological activity in general is a very unpredictable area. Note that in cases involving physiological activity such as the instant case, "the scope of enablement varies inversely with the degree of unpredictability of the factors involved". See In re Fisher, 427 F.2d 833, 839 (1970). Sepsis is caused by different bacteria, and there is no known method/compound in the art for the prevention of sepsis. Thus the skilled artisan would view that prophylaxis of severe sepsis in a patient in need of such treatment totally, absolutely or permanently is highly unpredictable using the compound of formula (I) or formula (II).

(8) The Quantity of Experimentation Necessary:

The specification fails to provide support for the prevention of sepsis. Nor does it provide information to practice the claimed invention, absent undue experimentation.

Genetech, 108 F. 3d at 1366 states that "a patent is not a hunting license. It is not a reward for search, but compensation for its successful conclusion" and "patent protection is granted in return for an enabling disclosure of an invention, not for vague intimations of general ideas that may or may not be workable."

Accordingly the claims are evaluated as an agent for the treatment of severe sepsis and a method of treating severe sepsis, and not a method of prophylaxis of severe sepsis.

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claim 6 is rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 6 is rejected, as they provide the use of a compound represented by the formula (I) or the formula (II) for the production of an agent for the treatment of severe sepsis, but, since the claim does not set forth any steps involved in the method/process, it is unclear what method/process applicant is intending to encompass. A claim is indefinite where it merely recites a use without any active, positive steps delimiting how this use is actually practiced.

Claims 1-6 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

The recitation, "pro-drug" of compound of formula (I) or formula (II) in these claims render claims herein indefinite. The recitation, "pro-drug" of the compounds of formula (I) or formula (II) is not clearly defined in the specification. Hence, one of ordinary skill in the art could not ascertain and interpret the metes and bounds of the patent protection desired as to "pro-drug" of compounds of formula (I) or formula (II) herein, since one of ordinary skill in the art would clearly recognize that many widely varying groups could possibly substituting the compounds herein would read on the "pro-drug" of the compounds.

Given the fact that any significant structural variation to a compound would be reasonably expected to alter its properties, e.g., physical, chemical, physiological effects and functions. Thus, it is unclear and indefinite as to the "pro-drug" of compounds herein encompassed thereby.

Claim Rejections - 35 USC § 101

35 U.S.C. 101 reads as follows:

> Whoever invents or discovers any new and useful process, machine, manufacture, or composition of matter, or any new and useful improvement thereof, may obtain a patent therefor, subject to the conditions and requirements of this title.

Claim 6 is rejected under 35 U.S.C. 101 because the claimed recitation of a use, without setting forth any steps involved in the process, results in an improper definition of a process, i.e., results in a claim which is not a proper process claim under 35 U.S.C. 101. See for example *Ex parte Dunki*, 153 USPQ 678 (Bd.App. 1967) and *Clinical Products, Ltd.* v. *Brenner*, 255 F. Supp. 131, 149 USPQ 475 (D.D.C. 1966).

Claim 6 is examined as the method of use claims for the preparation of medicament for the treatment of severe sepsis, and the following rejections are made.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 1-3, 5-6 are rejected under 35 U.S.C. 102(b) as being anticipated by Ichimori et al. (EP 1063228, PTO-1449)

Ichimori et al. teach a method of treating sepsis or septic shock by administering a compound of formula (Iaa) which is same as instant formula (I). See abstract. Compound 72 is specified as a preferred compound of formula (Iaa), where R1 is ethyl, R2 is hydrogen, Ar is 2-chloro-4- fluoro phenyl, and n is 2, both l- and d-type. See page 76, Table 1; pages 86-95, claims. A method of manufacturing an agent for treating septic shock is also disclosed. See page 41, paragraphs [0129]-[0132]; page 85 paragraph [0253]; claims 36, 37.

Thus, Ichimori et al. anticipates instant claims 1-3, 5-6.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claim 4 is rejected under 35 U.S.C. 103(a) as being obvious over Ichimori et al. (EP 1063228) as applied to claims 1-3, 5-6 above, in view of DeMarsh et al. (US Patent 5,714,469).

Ichimori et al. is applied as discussed above.

Ichimori et al. does not specifically teach an antibacterial drug.

DeMarsh et al. teach that ceftazidime is a known antimicrobial agent routinely used for the treatment of sepsis (col. 2, lines 47-52), where the effective amount being from 1.0 to 100 ng/kg/day (col. 8, lines 18-19, 40-41).

It would have been prima facie obvious to a person of ordinary skill in the art, at the time the claimed invention was made, to combine compound 72 as disclosed by Ichimori et al. with ceftazidime as disclosed by DeMarsh et al. for the same purpose of treating sepsis or septic shock. A person of ordinary skill in the art would have been motivated to combine compound 72 as disclosed by Ichimori et al. with ceftazidime as disclosed by DeMarsh et al. because: (1) Ichimori et al. teach compound 72 for treating sepsis or septic shock; and (2) DeMarsh et al. teach that ceftazidime is routinely used for treating sepsis or septic shock. Therefore, one of ordinary skill in the art would have had a reasonable expectation of success in treating sepsis or septic shock with the combination of compound 72 as disclosed by Ichimori et al. and ceftazidime as disclosed by DeMarsh et al.

"It is prima facie obvious to combine two compositions each of which is taught by the prior art to be useful for the same purpose, in order to form a third composition to be used for the very same purpose .... The idea of combining them flows logically from their having been individually taught in the prior art." In re Kerkhoven, 626 F.2d 846, 850, 205 USPQ 1069, 1072 (CCPA 1980).

Double Patenting

The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. See In re Goodman, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); In re Longi, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); In re Van Ornum, 686 F.2d 937,214 USPQ 761 (CCPA 1982); In re Vogel, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); and In re Thorington, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent is shown to be commonly owned with this application. See 37 CFR 1.130(b).

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

Claims 1-6 are provisionally rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 14, 31 of copending Application No. 10/433826. Although the conflicting claims are not identical, they are not patentably distinct from each other. One of ordinary skill in the art at the time of invention would have been motivated to employ compound of formula (I) with reasonable expectation of success of treating sepsis because a method for the treatment of severe sepsis by administering a compound of formula I is claimed in ‘826

This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

Claims 1-4 are provisionally rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 7-8 of U.S. copending Application No. 12/226446. Although the conflicting claims are not identical,

they are not patentably distinct from each other because they are both drawn to substantially overlapping compositions.

The compositions, in the application '446 and in the instant application are seen to be substantially overlapping. Therefore, the instant claims 1-4 are seen to be obvious over the claims 7-8 of application 12/226446.

This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented

Claims 1-6 are rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1-32 of U.S. Patent No. 6,495,604. Although the conflicting claims are not identical, they are not patentably distinct from each other. One of ordinary skill in the art at the time of invention would have been motivated to employ compound of formula (I) with reasonable expectation of success of treating sepsis because a method for the treatment of severe sepsis by administering a compound of formula I is claimed in '604.

Claims 1-4 are rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1-5 of U.S. Patent No. 7,078,540. Although the conflicting claims are not identical, they are not patentably distinct from each other because they are both drawn to substantially overlapping compositions.

The compositions, in the application '540 and in the instant application are seen to be substantially overlapping. Therefore, the instant claims 1-4 are seen to be obvious over the claims 1-5 of U.S. Patent No. 7,078,540.

Conclusion

No claims are allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Shobha Kantamneni whose telephone number is 571-272-2930. The examiner can normally be reached on Monday-Friday, 8am-5pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Sreeni Padmanabhan can be reached on 571-272-0629. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

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